

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Masayuki Tsuchiya et al.      Art Unit : 1656  
Serial No. : 09/830,144      Examiner : Sheridan L. Swope  
Filed : April 20, 2001      Confirmation No.: 9796  
Notice of Allowance Date: August 12, 2005  
Title : METHOD FOR SCREENING COMPOUNDS INHIBITING SIGNAL  
TRANSDUCTION THROUGH INFLAMMATORY CYTOKINES

**MAIL STOP ISSUE FEE**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

RESPONSE TO NOTICE OF ALLOWANCE

In response to the Notice of Allowance mailed August 12, 2005, enclosed are a completed issue fee transmittal form PTOL-85B, Comments on Statement of Reasons for Allowance, and a check for \$1430 for the required fee, including ten (10) patent copies.

Please apply any additional charges or credits to our Deposit Account No. 06-1050.

Respectfully submitted,

Date: Oct. 27, 2005

Reg. NO. 44,164  
fw Janis K. Fraser, Ph.D., J.D.  
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October 27, 2005  
Date of Deposit



- TGF- $\beta$  is a pleiotropic factor and acts on diverse tissue and cell types, not just the immune system. With respect to inflammation, TGF- $\beta$  may be both pro-inflammatory and anti-inflammatory. The balance between these two opposing activities is crucial to maintaining immunological homeostasis in the host. There are multiple receptors and signal transduction mediators for TGF- $\beta$  (McCartney-Francis et al., *Int. Rev. Immunol.* 16(5-6):553-80, 1998, and Letterio et al., *Annu. Rev. Immunol.* 16:137-61, 1998);
- TGF- $\beta$  enhances the ability of macrophages to produce IL-10 (Maeda et al., *J. Immunol.* 155(10):4926-32, 1995); and
- methods of systemically analyzing the structure and function of peptides (Wells et al., U.S. Patent No. 5,580,723).

Thus, TGF- $\beta$  has many different functions, including both pro-inflammatory and anti-inflammatory activities. There are multiple receptors and signal transduction mediators for these TGF- $\beta$  functions. Absent specific teachings, a person of ordinary skill would not be able to recognize which mediator of TGF- $\beta$  signal transduction is responsible for which of the diverse functions of TGF- $\beta$ . The cited references teach only that TAK1-TAB1 may mediate TGF- $\beta$  functions. Nothing in the cited references teaches the role of TAK1-TAB1 in TGF- $\beta$ -induced inflammation, let alone TGF- $\beta$ -induced expression of IL-1, IL-6, IL-10 and TNF. Therefore, there is no motivation or suggestion for a skilled artisan to combine the cited references and come to the conclusion that TAK1-TAB1 mediates the induction of IL-1, IL-6, IL-10 and TNF by TGF- $\beta$ , rather than another TGF- $\beta$  activity. The combined teaching also provides no reasonable expectation of success for the claimed invention, as, in view of the art, TAK1-TAB1 could have proven to be responsible for any of the numerous other TGF- $\beta$  functions instead of inflammation.

Accordingly, it would not have been obvious to test any compound that inhibits TAK1/TAB1 binding for inhibition of TGF- $\beta$ -induced expression of IL-1, IL-6, IL-10 and TNF.

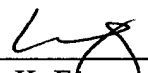
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Attorney's Docket No.: 14875-076001 / C1-005PCT-US

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